Complete Summary

GUIDELINE TITLE

Surveillance programs for early stage non-seminomatous testicular cancer.

BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Guideline Practice Initiative (CCOPGI). Surveillance programs for early stage non-seminomatous testicular cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2001 Jan [online update]. Various p. (Practice guideline; no. 3-5). [27 references]

Segal R, Lukka H, Klotz LH, Eady A, Bestic N, Johnston M, Genitourinary Cancer Disease Site Group, Cancer Care Ontario Practice Guidelines Initiative (CCOPGI). Surveillance programs for early stage non-seminomatous testicular cancer: a practice guideline. Can J Urol 2001 Feb;8(1):1184-92. [27 references]

COMPLETE SUMMARY CONTENT

SCOPE

DISEASE/CONDITION(S)

Non-seminomatous testicular cancer

GUIDELINE CATEGORY

Assessment of Therapeutic Effectiveness
Evaluation
Management
Risk Assessment
Treatment

CLINICAL SPECIALTY

Oncology
Radiation Oncology
Urology

INTENDED USERS

Physicians

GUIDELINE OBJECTIVE(S)

To determine what constitutes an appropriate surveillance program for men with clinical stage I non-seminomatous germ cell tumours of the testis (NSGCT)

TARGET POPULATION

Adult men with clinical stage I testicular cancer who are eligible for surveillance. Those eligible for surveillance are men with clinical stage I testicular cancer, as defined by a normal physical examination, normal radiological scans (computed tomography [CT]) and serum markers. These markers alpha-fetoprotein [AFP] and beta-subunit of human chorionic gonadotropin [betaHCG]) must be normal or fall within normal limits during their expected half-lives. If these criteria are not met, patients should not be offered surveillance.

INTERVENTIONS AND PRACTICES CONSIDERED

Surveillance Evaluation

1. Physical examination
2. Blood serum marker tests (alpha-fetoprotein and beta-subunit of human chorionic gonadotropin)
3. Chest x-ray
4. Computed tomography scan of abdomen and pelvis
5. Surveillance schedule

Relapse Treatment

1. Appropriate modality of therapy

MAJOR OUTCOMES CONSIDERED

Primary outcome

- Survival

Secondary outcomes

- Relapse rate
- Salvage rate for relapsed individuals

METHODOLOGY

METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)
Hand-searches of Published Literature (Secondary Sources)
Searches of Electronic Databases
Searches of Unpublished Data

DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

1999 Guideline

The MEDLINE and CANCERLIT databases were searched for the years 1988 to 1999 (April) using these medical subject headings: testicular neoplasms; neoplasms, germ cell and embryonal; neoplasm recurrence, local; recurrence; and follow-up studies. The following text words were also used: nonsemin: (or non semin:), follow:, or recur:. Methodological search terms were not used because the topic of surveillance was not well indexed in the databases and a broader strategy was required to identify potentially eligible studies. Relevant articles identified by the search, found in personal files or proceedings of meetings, e.g., American Society for Clinical Oncology (ASCO), or cited in papers and reviews were retrieved and reviewed. Additional bibliographies were searched and experts who are current in the field were interviewed.

The Physician Data Query database (U.S. National Cancer Institute) was also searched for both active and closed ongoing trials indexed with the diagnosis of stage I testicular cancer and the treatment modality of surgery.

2001 Update

The original literature search has been updated using MEDLINE and CANCERLIT databases (April 1999 through December 2000).

Inclusion and exclusion criteria

Randomized controlled trials (RCTs) comparing different surveillance strategies would provide the strongest evidence of superiority of one surveillance schedule over another, but none were found. One randomized controlled trial compared surveillance with adjuvant post-operative radiotherapy, however post-operative radiotherapy is not standard treatment. Thus, only the surveillance schedule from that trial was discussed in this overview. All prospective studies evaluating the surveillance of patients with clinical stage I non-seminomatous testicular cancer who received no adjuvant treatment were reviewed. The surveillance strategies used in the various studies were examined.

To be included in the analysis, the following criteria had to be met: (1) entry criteria for the study population must be defined, (2) details of the surveillance program must be available, (3) primary data on survival, relapse rate and/or salvage rate for relapsed patients must be reported, (4) no previous intervention or therapy must be permitted (radiotherapy or retroperitoneal lymph node

dissection, for example), and (5) the study must be published as a full report. All eligible studies were included, even if the selected patients had high-risk factors, such as embryonal cell histology and/or, vascular or lymphatic invasion. Thirteen studies were included in the final analysis. For practical reasons, studies were excluded if they were published in a language other than English.

A letter was sent to the first author of each study to ensure that the surveillance schedule was represented accurately in the published report. A follow-up paper for one study reported that the surveillance schedule was different in practice from the schedule described in the original report. The actual time between visits was, on average, twice as long as originally planned. For the purpose of the practice guideline report, the actual (rather than the planned) schedule was used. For all other studies, the published surveillance schedule (as confirmed by the first author of the study) was used.

NUMBER OF SOURCE DOCUMENTS

1999 Guideline

13 studies

2001 Update

4 studies (2 new studies and 2 that provided updated data for studies included in the original guideline document)

METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Expert Consensus (Committee)

RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Not applicable

METHODS USED TO ANALYZE THE EVIDENCE

Meta-Analysis of Summarized Patient Data
Systematic Review with Evidence Tables

DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

For the outcomes of relapse rate, salvage rate, and survival, the data were pooled by summing the number of events (relapse, response to salvage therapy, and deaths), and dividing these results by the total number of patients at risk. This number was converted to a percentage and the 95% confidence interval (CI) was calculated. The pooled values for both median follow-up time and median time to relapse in Table 3 of the original guideline document were calculated using the following equation:

Pooled median follow up =

$$\frac{m_1n_1 + m_2n_2 + m_3n_3 + \ldots}{N}$$

Where:

m = median follow-up time within a trial,

n = number of evaluable subjects within a trial,

N = number of subjects across trials

For two studies, there were incomplete analyses because not all of the patients had been evaluated. A letter was sent to each of these authors to ask for the final analysis. One author sent a paper in which the final results of the study were published. The other study was included in the pooled analysis using the existing data.

METHODS USED TO FORMULATE THE RECOMMENDATIONS

Expert Consensus

DESCRIPTION OF METHODS USED TO FORMULATE THE RECOMMENDATIONS

1999 Guideline

An earlier draft of the practice guideline report did not recommend one schedule over another because of the lack of evidence from randomized controlled trials (RCTs). After discussion, the Genitourinary Cancer Disease Site Group (DSG) decided that there should be a recommendation, based on the available evidence, regarding the type and frequency of tests used for surveillance. Although one schedule cannot be recommended as superior to another, there are common elements in the surveillance schedules described in the literature that can be used to guide decisions regarding surveillance.

Given that there were no differences in the event rates associated with the schedule of surveillance, one option would be to recommend the schedule with the minimum frequency of tests; this would cost less and be more convenient for the patient. Ultimately, the group considered the whole range of options presented and made recommendations that appeared to be clinically reasonable with respect to seeing patients more frequently rather than less frequently. Because relapse rate is highest within the first two years of follow-up, if relapse is detected early enough, then patients have a greater chance of being cured. Thus, a more aggressive schedule was recommended for the first two years in order to increase the likelihood of detecting early relapses. Although no randomized controlled trials have evaluated whether more frequent testing will ensure detection of early relapses, the DSG elected a more aggressive approach to maximize the chance of detecting recurrent disease as soon as possible.

The data do not suggest that beyond two years, the frequency of computed tomography (CT) scans of the abdomen and pelvis influences the outcomes. The

current standard of care is to do a CT scan at least every six months in the third year and once a year in the fourth and fifth year. This standard of care is based on recognition that 15% of recurrences are marker-negative, the natural history of the disease which suggests that abdominal recurrences do occur more than two years after presentation, and the fact that the prognosis is significantly better when abdominal masses are non-palpable. In addition, these patients are young and potentially curable. Therefore, the DSG felt that it was reasonable to recommend doing CT scans of the abdomen and pelvis every six months in the third year, and once a year in the fourth and fifth year.

When discussing comments from practitioner feedback, the DSG decided to clarify the patient population by recognizing that some patients are at a higher risk of relapsing than others. In recent years, post-orchiectomy treatment strategies, including surveillance, for patients with clinical stage I non-seminomatous germ cell testicular tumours have been accepted. Concurrently, additional efforts have been made to identify certain prognostic factors to identify patients who actually have pathological stage II disease, which is more likely to recur. To date, the most important prognostic factors (alone or in combination) for occult retroperitoneal disease appear to be the presence of lymphatic and/or vascular invasion and the presence of embryonal carcinoma in the primary specimen. When present in combination, the risk of occult disease is greater than if only a single risk factor is present and can exceed 50%. Thus, a point was added to the practice guideline recommendation to address patients who are at a higher risk of relapse.

2001 Update

The information above remains current.

RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

METHOD OF GUIDELINE VALIDATION

External Peer Review
Internal Peer Review

DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Practitioner feedback was obtained through a mailed survey of 176 practitioners in Ontario, consisting of nine questions asking for ratings on the quality of the draft recommendations and whether the recommendations should serve as a practice guideline. Written comments were invited. Follow-up reminders were sent at two weeks (post-card) and four weeks (second mailing of the full package). The Genitourinary Cancer Disease Site Group reviewed the results of the survey.

Final approval pf the original guideline report was obtained from the Practice Guidelines Coordinating Committee.

RECOMMENDATIONS

MAJOR RECOMMENDATIONS

- A recommended surveillance schedule is as follows:
  - Physical examination, blood serum marker tests (alpha-fetoprotein [AFP] and beta-subunit of human chorionic gonadotropin [betaHCG]), and chest x-rays should be conducted every month in the first year, every two months in the second year, every three months in the third year, and every six months in the fourth and fifth years;
  - Computed tomography (CT) scans of the abdomen and pelvis should be conducted every three months in the first year, every four to six months in the second year and every six months in the third year. Although the limited data available suggest that beyond two years the frequency of computed tomography scans of the abdomen and pelvis does not influence relapse rate, salvage rate and survival, the current standard of care should be maintained and computed tomography scans of the abdomen and pelvis should be performed at least every six months in the third year and once a year in the fourth and fifth year.
- Upon relapse, patients should be treated rapidly with the appropriate modality of therapy by a physician experienced in the treatment of non-seminomatous germ cell tumours of the testis.

CLINICAL ALGORITHM(S)

None provided

EVIDENCE SUPPORTING THE RECOMMENDATIONS

TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

1999 Guideline
There were no randomized trials comparing surveillance schedules. Thirteen studies were included for review: one randomized controlled trial compared surveillance alone with radiotherapy after orchiectomy and 12 case series followed patients in a surveillance program after orchiectomy.

2001 Update
Review and updating activities identified four relevant articles, two that were new studies and two that provided updated data for studies included in the original guideline report. The new information is consistent with information included in the original full-text guideline report.

BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

POTENTIAL BENEFITS

These guidelines may aid physicians in choosing appropriate surveillance programs for patients with early stage non-seminomatous testicular cancer.

POTENTIAL HARMS

There were no reported harms associated with any of the surveillance programs. However, this assumes that upon relapse, the appropriate modality of effective therapy was accepted by the patient and delivered.

QUALIFYING STATEMENTS

QUALIFYING STATEMENTS

- The presence of embryonal cell histology and/or vascular or lymphatic invasion is associated with an increased risk of relapse. This should be taken into consideration when selecting surveillance as the primary management option. Whether or not a patient is at high risk, the same recommended surveillance schedule applies.
- The physician and patient should discuss whether the patient is willing to follow a regular schedule of visits to determine whether surveillance is a suitable management option.
- Follow-up should be based on a regular schedule of visits with a physician in an environment that incorporates the principles of oncologic care with the support services (radiographic and hematologic) required for intensive surveillance of these individuals.

IMPLEMENTATION OF THE GUIDELINE

DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

IOM CARE NEED

Living with Illness

IOM DOMAIN

Effectiveness
Patient-centeredness

IDENTIFYING INFORMATION AND AVAILABILITY

BIBLIOGRAPHIC SOURCE(S)

Cancer Care Ontario Guideline Practice Initiative (CCOPGI). Surveillance programs for early stage non-seminomatous testicular cancer [full report]. Toronto (ON): Cancer Care Ontario (CCO); 2001 Jan [online update]. Various p. (Practice guideline; no. 3-5). [27 references]

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ADAPTATION

Not applicable: The guideline was not adapted from another source.

DATE RELEASED

1999 Jul 23 (updated online 2001 Jan)

GUIDELINE DEVELOPER(S)

Practice Guidelines Initiative - State/Local Government Agency [Non-U.S.]

GUIDELINE DEVELOPER COMMENT

The Practice Guidelines Initiative (PGI) is the main project of the Program in Evidence-based Care (PEBC), a Province of Ontario initiative sponsored by Cancer Care Ontario and the Ontario Ministry of Health and Long-Term Care.

SOURCE(S) OF FUNDING

Cancer Care Ontario, Ontario Ministry of Health and Long-Term Care

GUIDELINE COMMITTEE

Genitourinary Cancer Disease Site Group

COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Genitourinary Cancer Disease Site Group Members: Dr. H. Lukka, (Chair), Radiation Oncologist; Dr. J. Barkin, Urologist; Dr. G. Bauman, Radiation Oncologist; Dr. J. Bowen, Radiation Oncologist; Dr. M. Brundage, Radiation Oncologist; Dr. J. Chin, Urologist; Dr. R. Choo, Radiation Oncologist; Dr. J. Crook, Radiation Oncologist; Dr. L. Eapen, Radiation Oncologist; Dr. N. Fleshner, Urologist; Dr. L. Klotz, Urologist; *Dr. W. Love, Urologist; Dr. W. Orovan, Urologist; *Dr. H. Prichard, Radiation Oncologist; Dr. L. Reyno, Medical Oncologist; Dr. R. Segal, Medical Oncologist; Dr. T. Short, Urologist; Dr. J. Srigley, Medical Oncologist; Dr. J. Trachtenberg, Urologist; Dr. P. Warde, Radiation Oncologist; Dr. E. Winquist, Medical Oncologist; Two community representatives

Resource group members working with the Genitourinary Cancer Disease Site Group: Faculty: Dr. K. Pritchard; Staff: *A. Eady, *N. Bestic, B.R. Markman

*Members that have completed term with the Genitourinary Cancer Disease Site Group

FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Members of the Genitourinary Cancer Disease Site Group disclosed potential conflict of interest information.

GUIDELINE STATUS

This is the current release of the guideline.

The guideline developer instituted a new format for their guidelines and evidence summaries: A SUMMARY of the original Practice Guideline or Evidence Summary, integrated with the most current information, replaces the ABSTRACT, RECOMMENDATION, BRIEF REPORT and EVIDENCE UPDATE.

The FULL REPORT, initially the full original Guideline or Evidence Summary, over time will expand to contain new information emerging from their reviewing and updating activities.

Please visit the Cancer Care Ontario Web Site for details on any new evidence that has emerged and implications to the guidelines.

GUIDELINE AVAILABILITY

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

AVAILABILITY OF COMPANION DOCUMENTS

The following is available:

- Surveillance programs for early stage non-seminomatous testicular cancer. Summary. Toronto (ON): Cancer Care Ontario (CCO), 1999 Jul 23 (updated online 2001 Jan).

Electronic copies: Available in Portable Document Format (PDF) from the Cancer Care Ontario Web site.

PATIENT RESOURCES

None available

NGC STATUS

This summary was completed by ECRI on June 5, 2002. The information was verified by the guideline developer as of July 8, 2002.

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Date Modified: 5/10/2004